Table. (*Continued*)

	Total (%)
Yes	6 (16%)
No	31 (84%)
Myeloablative Conditioning	37 (100%)
Graft Source	
UCB	9 (24%)
MRD	15 (41%)
MURD	7 (19%)
MMURD	6 (16%)
HLA Match	
Match	20 (54%)
Mismatch	17 (46%)
CSA containing GVHD Prophylaxis	
Yes	29 (78%)
No	8 (22%)

*Cytogenetics not available for 1 patient

Results: Neutrophil engraftment occurred in 89% of patients at a median of 23 days (range 12-40). Patients transplanted after year 1999 were more likely to engraft (RR 2.27, p = .04). Overall survival (OS) was 70% and 53% at 1 and 3 years. In multivariate analysis (MVA), OS was increased in patients who did not receive pre HSCT chemotherapy (RR 0.04, p = .01) and decreased in those with an IPSS score of Int-2 (RR 11.96, p = .03). Disease free survival (DFS) was 62% and 48% at 1 and 3 years. In MVA, factors associated with improved DFS at 3 years include having secondary MDS (RR 0.13, p = .02), undergoing HSCT after 1999 (p = .02 at 3 years), not receiving pre HSCT chemotherapy (RR 0.06, p<.01), and a short interval (<140 days) from diagnosis to transplant (RR 0.21, p = .03). Those with an IPSS score of Int-2 had a significantly lower DFS (RR 3.96, p = .03). WHO classification, cytogenetics and pre HSCT blast percentage had no significant impact on either OS or DFS. The relapse rate at 2 years was 20%. Factors associated with decreased relapse include having secondary MDS (RR 0.04, p<.01) and not receiving pre HSCT chemotherapy (RR 0.21, p = .03). Treatment-related mortality (TRM) was 25% at 1 year. The risk of TRM was increased in patients with a pre HSCT blast count ≥ 5% (RR 6.65, p = .01) and was decreased in patients who did not receive pre HSCT chemotherapy (RR 0.07, P = .02). At 100 days the cumulative incidence of grades II-IV and III-IV acute graft versus host disease (GVHD) was 40% and 16%, respectively. The incidence of chronic GVHD at one year was 19%.

Conclusions: Our results suggest that in order to achieve optimal outcomes, children with MDS should be referred for allogeneic HSCT soon after diagnosis and that unlike in adult MDS, pre HSCT chemotherapy does not appear to improve outcomes.

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OUTCOME OF POOR RESPONSE PAEDIATRIC AML USING EARLY SCT

Wareham, N.E.[1], Heilmann, C.[1], Abrahamsson, J.[2], Forestier, E.[3], Gustafsson, B.[4], Ha, S.-Y.[5], Heldrup, J.[6], Jahnukainen, K.[7], Jónsson, Ó.G.[8], Lausen, B.[1], Palle, J.[9], Zeller, B.[10], Hasle, H.[11] [1] The University Hospital Rigshospitalet, Copenhagen, Denmark; [2] The Queen Silvia Children's Hospital, Gothenburg, Sweden; [3] University of Umeå, Umeå, Sweden; [4] Karolinska Institute, Karolinska University Hospital, Huddinge, Sweden; [5] Queen Mary Hospital, Hong Kong; [6] University Hospital Lund, Lund, Sweden; [7] Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; [8] University Hospital, Reykjavík, Iceland; [9] University Children's Hospital, Uppsala, Sweden; [10] Oslo University Hospital Rikshospitalet, Oslo, Norway; [11] Aarhus University Hospital Skejby, Aarhus, Denmark

Background: Children with poor response acute myeloid leukaemia (AML) or refractory AML are generally considered to have a very poor outcome. Allogeneic stem cell transplantation (SCT) has been recommended for these children however, the advantage of SCT as opposed to continuous chemotherapy is not clear. The aim of this study was to investigate survival for poor response AML patients treated with SCT.

Procedure: The patients were treated according to the NOPHO-AML 2004 protocol and data were collected from the NOPHO-AML database. All patients received AIET (Cytarabine, Idarubicin, Etoposide, Thioguanine) and AM (Cytarabine, Mitoxantrone) as induction therapy. Poor response was defined as more than 15% blasts on day 15 after AIET and/or >5% blasts after AM. These patients proceeded to allo-SCT if a donor (family or unrelated) was available.

Results: Twenty-five of 230 patients had a poor response. SCT was performed in 21, using unrelated donors in 16, matched sibling donors (MSD) in 4 and a haploidentical donor in one of the transplants. The median follow-up was 2.9 years (range 0.7-7.3) and 3-year probability of survival 89%. Of five patients with more than 5% blasts at time of SCT four remain alive.

Conclusions: The poor responders had a significantly better prognosis than has previously been reported for patients with high blast count on day 15 and it seems that SCT is the treatment of choice for children with poor response AML.

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EGF SIGNALING REGULATES HEMATOPOIETIC REGENERATION FOLLOWING TOTAL BODY IRRADIATION

Doan, P.L.[1], Russell, J.L.[1], Himburg, H.A.[1], Helms, K.[1], Sullivan, J.M.[2], Jeffords, L.B.[2], Chao, N.J.[1,4], Kirsch, D.G.[2,3], Chute, J.P.[1,3] [1] Duke University Medical Center, Durham, NC; [2] Duke University Medical Center, Durham, NC; [3] Duke University Medical Center, Durham, NC; [4] Duke University Medical Center, Durham, NC

VEGFR2+ sinusoidal endothelial cells are necessary for normal hematopoietic reconstitution following myelosuppressive chemo- or radiotherapy (Hooper et al, Cell Stem Cell 2009). However, the mechanisms through which BM endothelial cells promote HSC regeneration remain unknown. We developed a mouse model in which mice bearing cell-specific deletion of Bak and Bax in Tie2$^+$ cells (Tie2Cre;Bak1-/-;BaxFl/- mice) were irradiated with sublethal and lethal doses of total body irradiation to assess whether protection of BM Tie2$^+$ ECs from radiation-induced apoptosis could protect the hematopoietic compartment from myeloablative toxicity. Tie2Cre;Bak1-/-;BaxFL/- mice demonstrated protection of BM HSCs and 100% survival following lethal dose TBI (750 cGy), whereas mice that retained Bax expression in Tie2$^+$ cells demonstrated depletion of BM HSCs and only 10% survival (p<0.0001). To determine the mechanism through which Tie2$^+$ BM ECs regulate HSC regeneration, we performed a cytokine array screen of BM serum from Tie2Cre;Bak1-/-;BaxFl/- mice and compared with Tie2Cre;Bak1-/-;BaxFl/+ mice and C57Bl6 mice. Among several genes which were up- or down-regulated in the BaxFl/- mice, we found an 18-fold increase in the concentration of epidermal growth factor (EGF) compared to BaxFl/+ and C57Bl6 mice (p = 0.04). We then showed that BM ECs express EGFR and BM ckit+sca-1+lin- cells also express EGF in C57Bl6 mice. Interestingly, antibody blockade of EGF in vitro blocked the ability of BaxFl/- ECs to support HSC regeneration following 300 cGy irradiation. Furthermore, systemic administration of EGF to irradiated mice caused a profound recovery of BM HSC and progenitor cells compared to saline treated control mice. Similarly, administration of erlotinib, an EGFR antagonist, caused a significant delay in recovery of BM HSCs in mice following high dose irradiation. Mechanistic studies revealed that treatment of HSCs with EGF significantly increased EGFR phosphorylation and downstream activation of Akt signaling. Furthermore, inhibition of Akt signaling blocked the beneficial effect of EGF in mediating the recovery of HSCs following radiation exposure, suggesting that EGF action on HSC regeneration was mediated by Akt activation. These data demonstrate that EGF is an important regulator of HSC regeneration in vivo and a potential new target for therapies to accelerate hematopoietic reconstitution following chemotherapy and radiation exposure.